

PATENT 600-1-087CIP2I

Cp 1636  
#23  
JF**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE** **RECEIVED**

APPLICANT(S): Friedman et al.

AUG 18 1999

SERIAL NO.: 08/485,943

EXAMINER: Railey, J.

DATE FILED: June 7, 1995

ART UNIT : 1636

TECH CENTER 1600/2900

FOR: MODULATORS OF BODY WEIGHT CORRESPONDING NUCLEIC  
ACIDS AND PROTEINS, AND DIAGNOSTIC AND THERAPEUTIC  
USES THEREOF

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**INFORMATION DISCLOSURE STATEMENT**

In accordance with Applicant's and Applicant's representatives' Duty of Disclosure under 37 CFR § 1.56, and pursuant to 37 CFR § 1.97 and MPEP 717.05(b), Applicant submits herewith documentary information for consideration by the Examiner. Information herein cited is only set forth in fulfillment of Applicant's duty of candor in disclosing all information brought to his attention, and is not an admission that it can be used adversely. The publications forwarded herewith are listed on the enclosed Form PTO-1449. Applicant requests that the Examiner, upon reviewing the enclosed materials, initial the enclosed form and return a copy thereof in accordance with the instructions on the form.

In accordance with 37 C.F.R. §1.56 and §1.97, the references listed on the attached form PTO-1449 are being brought to the attention of the Examiner for consideration in connection with the examination of the above-identified patent application.

**Petition for Consideration of the Information Disclosure Statement Under 37 CFR § 1.97(d)**

Applicants hereby request consideration of the present information disclosure statement, which is being submitted after the mailing date of the Final Action under 37 CFR §1.113.

**Certification Under 37 C.F.R. § 1.97(e)(2) and § 1.98(d)**

The undersigned agent for applicants hereby certifies that no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application and, to the knowledge of the undersigned attorney has been considered on the record in co-pending comparison applications, wherefore copies of the references need not be submitted herewith.

**Fee**

The fee required for filing this information disclosure statement has been estimated to be \$130.00 (37 C.F.R. § 1.17(i)), and accordingly a check in this amount is enclosed. Please charge any additional fees, or credit any overpayments, to Klauber & Jackson Deposit Account 11-1153. A duplicate of this paper is being submitted for accounting purposes.

08/17/1999 SDJUNG 00000016 08485943

130.00 DP

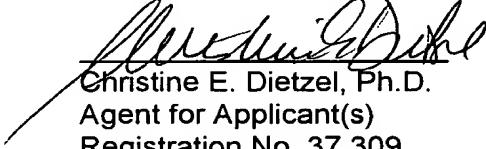
01 FC:122

Patent 600-1-087CIP2I

In as much as a copy of References **A25** through **C118** listed on the attached PTO Form-1449, have been provided to the Examiner, particularly with regard to 08/488,208 (our Reference 600-1-087CIP2B) they are not enclosed herewith. Should the Examiner wish a copy of any or all references, they will be promptly provided upon his request.

It is respectfully requested that the Examiner make these references of record, and to indicate consideration thereof by returning a copy of the attached form PTO-1449 with initials or other appropriate marks.

Respectfully submitted,



Christine E. Dietzel, Ph.D.  
Agent for Applicant(s)  
Registration No. 37,309

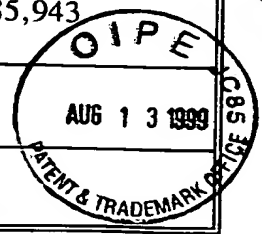
KLAUBER & JACKSON  
411 Hackensack Avenue  
Hackensack, New Jersey 07601  
(201)487-5800

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943

## INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636

## U.S. PATENT DOCUMENTS

*Examiner Initials		Document Number	Issue Date	Name	Class	Subclass	Filing Date If Appropriate
	A25	5,073,627	12/17/91	Curtis <i>et al.</i>	530	351	
	A26	5,116,964	05/26/92	Capon <i>et al.</i>	536	27	
	A27	5,225,538	07/06/93	Capon <i>et al.</i>	530	387.3	
	A28	5,359,034	10/25/94	Skelly <i>et al.</i>	530	351	
	A29	5,428,130	06/27/95	Capon <i>et al.</i>	530	350	
	A30	5,447,851	09/05/95	Beutler <i>et al.</i>	435	69.7	
	A31	5,455,165	10/03/95	Capon <i>et al.</i>	435	64.7	
	A32	5,480,981	01/02/96	Goodwin <i>et al.</i>	536	23.5	
	A33	5,514,582	05/07/96	Capon <i>et al.</i>	435	252.3	
	A34	5,574,018	11/12/96	Habberfield <i>et al.</i>	514	21	
	A35	5,670,625	09/23/97	Lyman <i>et al.</i>	530	387.3	
	A36	5,714,147	02/03/98	Capon <i>et al.</i>	424	178.1	
	A37	5,719,266	02/17/98	DiMarchi <i>et al.</i>	530	350	
	A38	5,739,277	4/14/98	Presta <i>et al.</i>	530	326	
	A39	5,756,461	05/26/98	Stephens, T.W.	514	12	
	A40	5,827,734	10/27/98	Weigle <i>et al.</i>	435	325	

EXAMINER

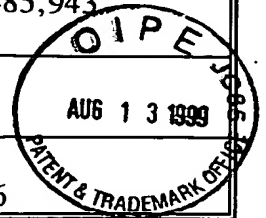
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeApp. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**FOREIGN PATENT DOCUMENTS**

*Examiner Initials		Document Number	Publication Date	Country	Class	Subclass	Translation	
							Yes	No
	B78	AU-B-51978/96	11/14/96	AU				
	B79	EP 0 401 384	12/12/90	EP				
	B80	WO 83/04053	11/24/83	WIPO				
	B81	WO 89/10932	11/16/89	WIPO				
	B82	WO 94/20069	09/15/94	WIPO				
	B83	WO 95/21629	08/17/95	WIPO				
	B84	WO 96/03141	02/08/96	WIPO				
	B85	WO 96/04388	02/15/96	WIPO				
	B86	WO 96/05309	02/22/96	WIPO				
	B87	WO 96/11953	04/25/96	WIPO				
	B88	WO 96/18412	06/20/96	WIPO				
	B89	WO 96/29989	10/03/96	WIPO				
	B90	WO 97/24137	07/10/97	WIPO				

**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, etc.)

C1	Altman, S.W. <i>et al.</i> , "Expression and Purification of a Synthetic Human Obese Gene Product," <i>Protein Expression and Purification</i> , 6:722-726 (1995).
----	--

EXAMINER

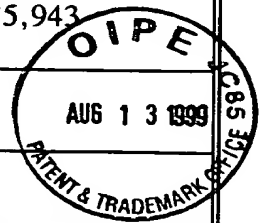
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, etc.)

C11	Angier, N., "Researchers Link Obesity In Humans To Flaw In A Gene," <i>The New York Times</i> reported on December 1, 1994.
C3	Barinaga, " 'Obese' Protein Slims Mice", <i>Science</i> , 269:475-476 (July, 1995).
C4	Baron, M.H. <i>et al.</i> , "Antibodies against the Chemically Synthesized Genome-Linked Protein of Poliovirus React with Native Virus-Specific Proteins," <i>Cell</i> , 28:395-404 (February, 1982).
C5	Bennett, B.D. <i>et al.</i> , "A role for leptin and its cognate receptor in hematopoiesis," <i>Current Biology</i> , 6(9):1170-1180 (September 1, 1996).
C6	Bishop, J.E., "Newfound Gene May Control Fat Storage," <i>The Wall Street Journal, Health and Science</i> , reported on December 1, 1994.
C7	Bishop, J.E., "Rockefeller Study Supports Theory That Body Has Fat-Maintenance System," <i>Wall Street Journal</i> , reported on March 9, 1995.
C8	Campfield, L.A. <i>et al.</i> , "Strategies and Potential Molecular Targets for Obesity Treatment," <i>Science</i> , 280:1383-1387 (May, 1998).
C9	Capon, D.J. <i>et al.</i> , "Designing CD4 immunoadhesins for AIDS therapy," <i>Nature</i> , 337:525-531 (February, 1989).
C10	Chen, H. <i>et al.</i> , "Evidence That the Diabetes Gene Encodes the Leptin Receptor: Identification of a Mutation in the Leptin Receptor Gene in <i>db/db</i> Mice," <i>Cell</i> , 84:491-495 (February, 1996).
C11	Cioffi, J.A. <i>et al.</i> , "Novel B219/OB receptor isoforms: Possible role of leptin in hematopoiesis and reproduction," <i>Nature Medicine</i> , 2(5):585-589 (May, 1996).
C12	Coleman, D.L. <i>et al.</i> , "The Influence of Genetic Background on the Expression of the Obese ( <i>Ob</i> ) Gene in the Mouse," <i>Diabetologia</i> , 9:287-293 (1973).
C13	Comuzzie, A.G. <i>et al.</i> , "The Search for Human Obesity Genes," <i>Science</i> , 280:1374-1377 (May, 1998).

EXAMINER

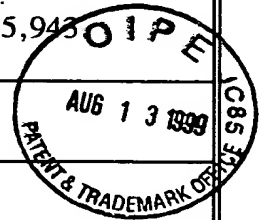
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C14	Considine, R. V. <i>et al.</i> , "Ob Gene Expression Is Increased in Adipocytes from Obese Humans," <i>Diabetes</i> , 44:202A (May, 1995) (ABSTRACT 739).
C15	Cusin I. <i>et al.</i> , "The <i>ob</i> Gene and Insulin A Relationship Leading to Clues to the Understanding of Obesity," <i>Diabetes</i> , 44:1467-1470 (December, 1995).
C16	Detjen, J. (Philadelphia Inquirer), "Obesity gene find may help millions someday," <i>The Durham Herald Co., The Herald-Sun</i> (Durham, NC), pg. A1, reported on December 1, 1994.
C17	Dressman, G. R. <i>et al.</i> , "Antibody to hepatitis B surface antigen after a single inoculation of uncoupled synthetic HbsAg peptides," <i>Nature</i> , 295:158-160 (January, 1982).
C18	Ellison, J. W. <i>et al.</i> , "The nucleotide sequence of a human immunoglobulin C $\gamma$ 1 gene," <i>Nucleic Acids Research</i> , 10(13):4071-4079 (1982).
C19	Enerbäck, S. <i>et al.</i> , "Mice lacking mitochondrial uncoupling protein are cold-sensitive but not obese," <i>Nature</i> , 387:90-93 (May, 1997).
C20	Evans, D. J. <i>et al.</i> , "Relationship of Body Fat Topography to Insulin Sensitivity and Metabolic Profiles in Premenopausal Women," <i>Metabolism</i> , 33(1):68-75 (January, 1984).
C21	Ferré, P., "Obésité. Produit de Gène <i>ob</i> Et Contrôle De La Masse Adipeuse [Obesity, The <i>ob</i> Gene Product and Control of Adipose Mass]," <i>Diabète &amp; Metabolisme (Paris)</i> , 21:217-218 (1995).
C22	Fisher, C. J. <i>et al.</i> , "Treatment of Septic Shock with the Tumor Necrosis Factor Receptor:Fc Fusion Protein," <i>N. Engl. J. Med.</i> , 334:1697-1702 (1996).
C23	Flam, "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Science</i> , 266:1477-1478 (December, 1994).

EXAMINER

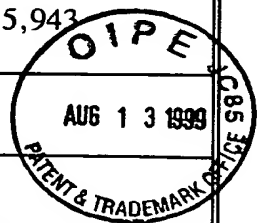
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C29	Ford, C.F. <i>et al.</i> , "Fusion Tails for the Recovery and Purification of Recombinant Proteins," <i>Protein Expression and Purification</i> , 2:95-107 (1991).
C25	Frederich, R. <i>et al.</i> , "Nutritional Regulation of ob Gene mRNA in White Adipose Tissue," The Endocrine Society, Programs & Abstracts, 77th Meeting, June 14-17, 1995, Washington, D.C., p.173 (ABSTRACT OR25-3)
C26	Frederich R.C. <i>et al.</i> , "Leptin levels reflect body lipid content in mice: Evidence for diet-induced resistance to leptin action," <i>Nature Medicine</i> , 1(12):1311-1314 (December, 1995).
C27	GenBank Accession No. 603288, ob, Deposited by Zhang <i>et al.</i> , March 30, 1995.
C28	GenBank Accession No. 623332, ob, Deposited by Zhang <i>et al.</i>
C29	GenBank Accession No. 726297, obesity protein, Deposited by Chehab <i>et al.</i> , March 21, 1995.
C30	GenBank Accession No. U18812, Mus musculus obese precursor (ob) mRNA, complete cds., deposited by Zhang, Y. <i>et al.</i> , March 30, 1995.
C31	GenBank Accession No. U18915, Human obese (ob) mRNA, complete cds., deposited by Zhang, Y. <i>et al.</i> , January 13, 1995.
C32	GenBank Accession No. U22421, Mus musculus obesity protein (ob) gene, complete cds., Deposited by Chehab <i>et al.</i> , March 23, 1995.
C33	Grundy and Barnett, "Metabolic and Health Complications of Obesity," <i>Disease-a- Month (DM)</i> , 36:645-696 (December, 1990)
C34	Gura, T., "Uncoupling Proteins Provide New Clue to Obesity's Causes," <i>Science</i> , 280:1369-1370 (May, 1998).

EXAMINER

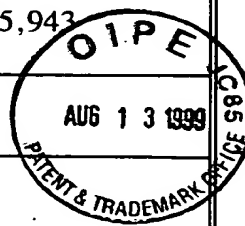
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, etc.)

C35	Hamilton, B.S. <i>et al.</i> , "Increased obese mRNA expression in omental fat cells from massively obese humans," <i>Nature Medicine</i> , 1(9):953-956 (September, 1995).
C36	Harvill, E.T. <i>et al.</i> , "An IgG3-IL2 fusion protein activates complement, binds FcγRI, generates LAK activity and shows enhanced binding to the high affinity IL-2R," <i>Immunotechnology</i> , 1:95-105 (1995).
C37	Hawkes, N. "Obesity of Mice and Men," Times Newspaper Limited, <i>The Times</i> , reported on December 5, 1994.
C37	He, Y. <i>et al.</i> , "The Mouse <i>obese</i> Gene," <i>Journal of Biological Chemistry</i> , 270(48):28887-28891 (December, 1995).
C36	Helm, L. (Times Staff Writer), "Gene Found That May Lead To Obesity," <i>The Times Mirror Company, Los Angeles Times, part A, page 1, col. 3</i> (December 1, 1994).
C40	Henry R.R. <i>et al.</i> , "Effects of Weight Loss on Mechanisms of Hyperglycemia in Obese Non-Insulin-Dependent Diabetes Mellitus," <i>Diabetes</i> , 35:990-998 (September, 1986).
C41	Highfield, R. (Science Editor), "Scientists find cause of fat mice and men Gene discovery from overweight rodents may help to produce drugs for people with a hereditary risk of obesity," <i>Telegraph Group Limited, The Daily Telegraph</i> , pg. 7 (December 1, 1994).
C42	Hill, J.O. <i>et al.</i> , "Environmental Contributions to the Obesity Epidemic," <i>Science</i> , 280:1371-1374 (May, 1998).
C43	Hirsch, J., "Some heat but not enough light," <i>Nature</i> , 387:27-28 (May, 1997).
C44	Hodgson, " 'Obesity' Where Less is More," <i>Bio/Technology</i> , 13:1060-1063 (October, 1995).

EXAMINER

DATE CONSIDERED

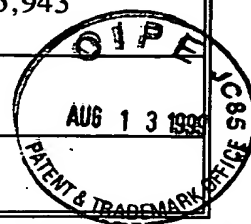
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, etc.)

C45	Hulsey, M.G. <i>et al.</i> , "An Anorectic Agent From Adipose Tissue of Overfed Rats: Effects of Feeding Behavior," <i>Physiol. &amp; Behav.</i> , 52:1141-1149 (1992).
C46	Hummel, K.P. <i>et al.</i> , "Diabetes, a New Mutation in the Mouse," <i>Science</i> , 153:1127-1128 (1966)
C47	Huse, W.D. <i>et al.</i> , "Generation of a Large Combinatorial Library of the Immunoglobulin Repertoire in Phage Lambda," <i>Science</i> , 246:1275-1281 (December, 1989).
C48	IBI FLAG BIOSYSTEM, "High Yield Expression, Detection, and Purification of Recombinant Proteins in E. coli," Integrated Sciences Pty Ltd, Sydney, Australia
C49	IBI FLAG Epitope, A Technical Bulletin for Users of FLAG Technology, International Biotechnologies Inc., FLAG Product Development Group, IBI, A Kodak Company, New Haven, CT, Volume 1, Number 1, pp. 1-24 (September, 1992).
C50	Iida, M. <i>et al.</i> , "Substitution at Codon 269 (Glutamine→Proline) of the Leptin Receptor (OB-R) cDNA Is the Only Mutation Found in the Zucker Fatty ( <i>fa/fa</i> ) Rat," <i>Biochemical and Biophysical Research Communications</i> , 224:597-604 (July 16, 1996).
C51	Ikeda, H. <i>et al.</i> , "Effects of Pioglitazone on Glucose and Lipid Metabolism in Normal and Insulin Resistant Animals," <i>Arzneim.-Forsch./Drug Res.</i> , 40 (I), Nr. 2:156-162 (1990).
C52	Isse N. <i>et al.</i> , "Structural Organization and Chromosomal Assignment of the Human obese Gene," <i>J. Biological Chemistry</i> , 270(46):27728-27733 (November, 1995).
C53	Iwanishi, M. <i>et al.</i> , "Effect of Pioglitazone on Insulin Receptors of Skeletal Muscles From High-Fat-Fed Rats," <i>Metabolism</i> , 42(8):1017-1021 (August, 1993).

EXAMINER

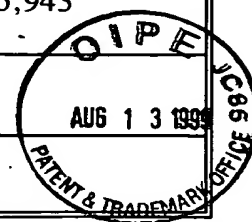
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C54	Jeanrenaud, B., "An hypothesis on the aetiology of obesity: dysfunction of the central nervous system as a primary cause," <i>Diabetologia</i> , 28:502-513 (1985).
C55	Jeanrenaud, B., "Central Nervous System and Peripheral Abnormalities: Clues to the Understanding of Obesity and NIDDM, <i>Diabetologia</i> , 37(Suppl. 2):S169-S178 (1994).
C56	Jeanrenaud, B. "Neuroendocrine and Metabolic Basis of Type II Diabetes as Studied in Animal Models," <i>Diabetes/Metabolism Reviews</i> , 4(6):603-614 (1988).
C57	Kaiser, E.T. <i>et al.</i> , "Amphiphilic Secondary Structure: Design of Peptide Hormones," <i>Science</i> , 223:249-255 (January, 1984).
C58	Kallen, C.B. <i>et al.</i> , "Antidiabetic thiazolidinediones inhibit leptin ( <i>ob</i> ) gene expression in 3T3-L1 adipocytes," <i>Proc. Natl. Acad. Sci.</i> , 93:5793-5796 (June, 1996).
C59	Kiberstis, P.A. <i>et al.</i> , "Regulation of Body Weight," <i>Science</i> , 280:1363 (May, 1998).
C60	Kissebah, A.H. <i>et al.</i> , "Health Risks of Obesity," <i>Medical Clinical North America</i> , 73(1):111-138 (January, 1989).
C61	Kissebah, A.H. <i>et al.</i> , "Regional Adiposity & Morbidity" in <i>Physiological Reviews: Body Fat Distribution &amp; Morbidity</i> , 74(4):761-811 (October, 1994).
C62	Kletzien, R.F. <i>et al.</i> , "Adipocyte Fatty Acid-Binding Protein: Regulation of Gene Expression <i>In Vivo</i> and <i>In Vitro</i> by an Insulin-Sensitizing Agent," <i>Molecular Pharmacology</i> , 42:558-562 (1992).
C63	Kobayashi, M. <i>et al.</i> , "Pioglitazone Increases Insulin Sensitivity by Activating Insulin Receptor Kinase," <i>Diabetes</i> , 41:476-483 (April, 1992).
C64	Köhler, G. <i>et al.</i> , "Derivation of specific antibody-producing tissue culture and tumor lines by cell fusion," <i>Eur. J. Immunol.</i> , 6:511-519 (1976).

EXAMINER

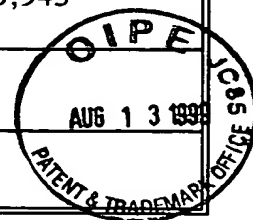
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C65	Lerner, R.A. <i>et al.</i> , "Antibodies to Chemically Synthesized Peptides Predicted from DNA Sequences as Probes of Gene Expression," <i>Cell</i> , 23:309-310 (February, 1981).
C66	Lerner, R.A. <i>et al.</i> , "Chemically synthesized peptides predicted from the nucleotide sequence of the hepatitis B virus genome elicit antibodies reactive with the native envelope protein of Dane particles," <i>Proc. Natl. Acad. Sci., USA</i> , 78(6):3403-3407 (June, 1981).
C67	Lerner, R.A., "Synthetic Vaccines," <i>Scientific American</i> , 248:66-74 (1983).
C68	Levin, N. <i>et al.</i> , "Decreased food intake does not completely account for adiposity reduction after ob protein infusion," <i>Proc. Natl. Acad. Sci.</i> , 93:1726-1730 (February, 1996).
C69	LindPaintner, K., "Clinical Implications of Basic Research: Finding an Obesity Gene-A Tale of Mice and Man," <i>New England Journal of Medicine</i> , 332(10):679-680 (March, 1995).
C70	Marx, J., "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Surg. Neurol.</i> , 43:351-352 (1995).
C71	Marx, J., "Obesity Gene Discovery May Help Solve Weighty Problem," <i>Science</i> , 266:1477-1478 (December, 1994).
C72	Masuda, K. <i>et al.</i> , "Effects of Troglitazone (CS-045) on insulin secretion in isolated rat pancreatic islets and HIT cells: an insulinotropic mechanism distinct from glibenclamide," <i>Diabetologia</i> , 38:24-30 (1995).
C73	Masuzaki <i>et al.</i> , "Molecular Cloning of a Rat Obese (ob) Complement DNA - Augmented Gene Expression in Obese-Hyperglycemic Wistar Fatty Rats," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.175 (ABSTRACT P1-250)

EXAMINER

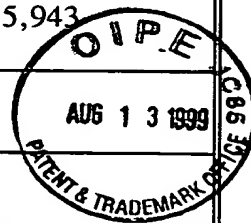
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C74	Masuzaki, H. <i>et al.</i> , "Adipose Tissue-specific Expression of the <i>Obese</i> (ob) Gene in Rats and Its Marked Augmentation in Genetically Obese-hyperglycemic Wistar Fatty Rats," <i>Proceedings of the Japan Academy Series B Physical and Biological Sciences</i> , 71(5):148-152 (1995).
C75	McGarry, J.D., "Does leptin lighten the problem of obesity?" <i>Current Biology</i> , 5(12):1342-1344 (1995).
C76	Mini-Symposium on Flag Technology, ASCB 1992, "Purification and Characterization of Cellular Proteins with the Flag Epitope," Colorado Convention Center, Denver, Colorado, 8 pages (November 18, 1992)
C77	Mizuno, T. <i>et al.</i> , "Elevated Expression of Obese (ob/ob) Gene Product in Adipose Tissue, and Impaired Induction by Insulin of Jun-B mRNA in Liver, in Genetically Obese Yellow Mice," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.174 (ABSTRACT P1-248)
C78	Moinat, M. <i>et al.</i> , "Modulation of <i>obese</i> gene expression in rat brown and white adipose tissues," <i>FEBS Letters</i> , 373:131-134 (1995).
C79	Murakami, N. <i>et al.</i> , "Amelioration of insulin resistance in genetically obese rodents by M16209, a new antidiabetic agent," <i>European Journal of Pharmacology</i> , 304:129-134 (1996).
C80	Murakami, T. <i>et al.</i> , "Cloning of Rat <i>Obese</i> cDNA and its Expression in Obese Rats," <i>Biochemical and Biophysical Research Communications</i> , 209(3):944-952 (April, 1995).
C81	Nakamura, M.T., "Another Obese Gene Function," <i>Nature</i> , 374:124 (March, 1995)

EXAMINER

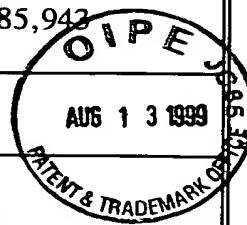
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,942**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C82	Ogawa, et al., Region-Specificities of the Obese (ob) Gene Expression in Adipose Tissue in Mice and Altered Gene Expression in C57BL/6J ob/ob Mice," Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., p.175 (ABSTRACT P1-249).
C83	Olefsky, J.M., "Weighing in on the Lean Genes," <i>Journal of Clinical Investigations</i> , 95:2427-2428 (June, 1995).
C84	Palmiter, R.D. <i>et al.</i> , "Metallothionein-Human GH Fusion Genes Stimulate Growth of Mice," <i>Science</i> , 222:809-814 (November, 1983).
C85	Peiris, A.N. <i>et al.</i> , "Glucose Metabolism in Obesity: Influence of Body Fat Distribution," <i>J. Clinical Endocrinology Metabolism</i> , 67(4):760-767 (1988).
C86	Peiris, A.N. <i>et al.</i> , "Relationship of Body Fat Distribution to the Metabolic Clearance of Insulin in Premenopausal Women," <i>International J. Obesity</i> , 11:581-589 (1987).
C87	Peiris, A.N. <i>et al.</i> , "Splanchnic Insulin Metabolism in Obesity Influence of Body Fat Distribution," <i>J. Clin. Invest.</i> , 78:1648-1657 (December, 1986).
C88	Polonsky, K.S. <i>et al.</i> , "Use of Biosynthetic Human C-peptide in the Measurement of Insulin Secretion Rates in Normal Volunteers and Type I Diabetic Patients," <i>J. Clin. Invest.</i> , 77:98-105 (January, 1986).
C89	Reddy, R. et al., "Equivalent Levels of OB Gene Expression in Adipose Tissues of Morbidly Obese and Lean Patients," The Endocrine Society, Programs & Abstracts, 77th Annual Meeting, June 14-17, 1995, Washington, D.C., (ABSTRACT P3-266).
C90	Rink, "In Search of a Satiety Factor," <i>Nature</i> , 372(1):406-407 (December, 1994).

EXAMINER

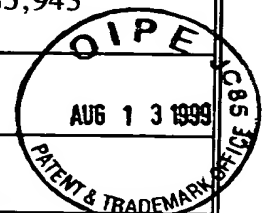
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C91	Schwartz, M.W. <i>et al.</i> , "Specificity of Leptin Action on Elevated Blood Glucose Levels and Hypothalamic Neuropeptide Y Gene Expression in ob/ob Mice," <i>Diabetes</i> , 45:531-535 (April, 1996).
C92	Shafir, E., "Animal Models of Non-Insulin-Dependent Diabetes," <i>Diabetes/Metabolism Reviews</i> , 8(3):179-208 (1992).
C93	Shigemoto, M. <i>et al.</i> , "Tissue Distribution of the Obese (ob) Gene Expression in Mice and Augmented Gene Expression in the ob/ob Mice," <i>Diabetes</i> , 44:204A (May, 1995) (ABSTRACT 748).
C94	Sohda, T. <i>et al.</i> , "Studies on Antidiabetic Agents. XII. <sup>1</sup> ) Synthesis and Activity of the Metabolites of (±)-5-[p-[2-(5-Ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione (Pioglitazone)," <i>Chem. Pharm. Bull.</i> , 43(12):2168-2172 (1995).
C95	Stephens <i>et al.</i> , "The Role of Neuropeptide Y in the Antiobesity Action of the Obese Gene Product," <i>Nature</i> , 377:530-532 (October, 1995).
C96	Stirling B. <i>et al.</i> , "Identification of Microsatellite Markers Near the Human ob Gene and Linkage Studies in NIDDM-Affected Sib Pairs," <i>Diabetes</i> , 44: 999-1001 (August, 1995).
C97	Sugiyama, Y. <i>et al.</i> , "Effects of Pioglitazone on Glucose and Lipid Metabolism in Wistar Fatty Rats," <i>Arzneim.-Forsch./Drug Res.</i> 40(1), Nr.3:263-267 (1990).
C98	Sugiyama, Y. <i>et al.</i> , "Effects of Pioglitazone on Hepatic and Peripheral Insulin Resistance in Wistar Fatty Rats," <i>Arzneim.-Forsch./Drug Res.</i> 40(1), Nr.4:436-440 (1990).
C99	Swanson, M.L. <i>et al.</i> , "Antidiabetic Agent Pioglitazone Increases Insulin Receptors on 3T3-L1 Adipocytes," <i>Drug Development Research</i> , 35: 69-82 (1995).

EXAMINER

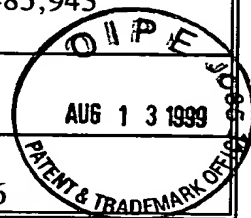
DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, etc.)

	C106	Tartaglia, L.A. <i>et al.</i> , "Identification and Expression Cloning of a Leptin Receptor, OB-R," <i>Cell</i> , 83:1263-1271 (December, 1995).
	C101	Taubes, G., "As Obesity Rates Rise, Experts Struggle to Explain Why," <i>Science</i> , 280:1367-1368 (May, 1998).
	C102	Thomas, S.A. <i>et al.</i> , "Thermoregulatory and metabolic phenotypes of mice lacking noradrenaline and adrenaline," <i>Nature</i> , 387:94-97 (May, 1997).
	C103	Van Zee, K. <i>et al.</i> , "Protection Against Lethal Escherichia coli Bacteremia in Baboons ( <i>Papio anubis</i> ) by Pretreatment with a 55-kDa TNF Receptor (CD120a)-Ig Fusion Protein, Ro 45-2081 <sup>1</sup> ," <i>The Journal of Immunology</i> , 156:2221-2230 (1996).
	C104	Vydelingum S. <i>et al.</i> , "Overexpression of the Obese Gene in the Genetically Obese JCR:LA-Corpulent Rat," <i>Biochemical and Biophysical Research Communications</i> , 216(1):148-153 (November, 1995).
	C105	Walsh, B.T. <i>et al.</i> , "Eating Disorders: Progress and Problems," <i>Science</i> , 280:1387-1390 (May, 1998).
	C106	Watson, T., "What really plumps you up," <i>U.S. News and World Report</i> , Vol. 117, No. 23, pg. 80, reported on December 12, 1994.
	C107	Weigle, D.S., "Appetite and the regulation of body composition," <i>FASEB</i> , 8:302-310 (1994).
	C102	Weigle <i>et al.</i> , "Recombinant <i>ob</i> Protein Reduces Feeding and Body Weight in the <i>ob/ob</i> Mouse," <i>J. Clin. Invest.</i> , 96:2065-2070 (October, 1995).
	C109	West, D.B. <i>et al.</i> , "Genetics of Dietary Obesity in AKR/J X SWR/J Mice - Segregation of the Trait and Identification of a Linked Locus on Chromosome-4," <i>Mammalian Genome</i> , 5(9):546-552 (September, 1994).
	C110	Wickelgren, I., "Obesity: How Big a Problem?" <i>Science</i> , 280:1364-1367 (May, 1998).

EXAMINER

DATE CONSIDERED

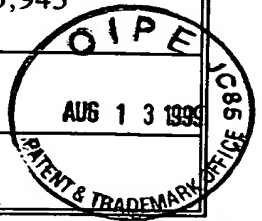
\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449 (Modified)

U.S. Department of Commerce  
Patent and Trademark OfficeAtty. Docket No.  
600-1-087CIP2ISerial No.  
08/485,943**INFORMATION DISCLOSURE STATEMENT**

(Use several sheets if necessary)

Applicant  
Friedman, J. *et al.*Filing Date  
June 7, 1995Group  
1636**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)**

C111	Willson, T.M. <i>et al.</i> , "The Structure-Activity Relationship between Peroxisome Proliferator-Activated Receptor $\gamma$ Agonism and the Antihyperglycemic Activity of Thiazolidinediones," <i>J. Med. Chem.</i> , 39:665-668 (1996).
C112	Wilson, B.E. <i>et al.</i> , "Identification of an overfeeding-induced adipocyte 5kb mRNA Lacking Sequence Homology to Known Adipocyte Genes," <i>The Adipose Cell: A Model for Integration of Hormone Signalling in the Regulation of Cellular Function</i> , p. 34 (ABSTRACT CA 318).
C114	Woods, S.C. <i>et al.</i> , "Signals That Regulate Food Intake and Energy Homeostasis," <i>Science</i> , 280:1378-1383 (May, 1998).
C114	Yamakawa, T. <i>et al.</i> , "Augmented Production of Tumor Necrosis Factor- $\alpha$ in Obese Mice," <i>Clinical Immunol. Immunopathol.</i> , 75(1):51-56 (April, 1995).
C115	Zarjevski <i>et al.</i> , "Chronic Intracerebroventricular Neuropeptide-Y Administration to Normal Rats Mimics Hormonal and Metabolic Changes of Obesity," <i>Endocrinology</i> , 133(4):1753-1758 (1993).
C116	Zhang, B. <i>et al.</i> , "Down-regulation of the Expression of the <i>Obese</i> Gene by an Antidiabetic Thiazolidinedione in Zucker Diabetic Fatty Rats and <i>db/db</i> Mice," <i>J. Biological Chemistry</i> , 271(16):9455-9459 (April, 1996).
C117	Zheng, X. <i>et al.</i> , "Administration of Noncytolytic IL-10/Fc in Murine Models of Lipopolysaccharide-Induced Septic Shock and Allogeneic Islet Transplantation," <i>The Journal of Immunology</i> , 154:5590-5600 (1995).
C118	Zucker, L.M. <i>et al.</i> , "Fatty, A New Mutation in the Rat," <i>J. Heredity</i> , 52:275-278 (1961).

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.